Original Article

Modification of Electrophysiological Properties of Pulmonary Veins and Adjacent Left Atrial Tissue by Radiofrequency Thermal Balloon Circumferential Ablation around the Pulmonary Vein Ostia: Correlation with Non-recurrence of Atrial Fibrillation

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Objective: The purpose of this study was to provide detailed information as to the modification of electrophysiological properties of pulmonary veins (PVs) and adjacent left atrial (LA) tissue caused by circumferential ablation (ABL) of superior and inferior pulmonary vein ostia using a novel radio-frequency balloon catheter (RBC), and to correlate such changes with recurrence or non-recurrence of atrial fibrillation (AF).

Background: Although isolation of the triggering foci in PVs using conventional ABL techniques is useful in the treatment of AF, ABL of PVs per se is time consuming and tends to be associated with high AF recurrence rate.

Methods and Results: Forty-nine patients with AF refractory to antiarrhythmic medication underwent circumferential ablation of PV-LA junction by RBC. Post ablation changes in electrophysiological properties around the PV ostia were studied with a basket catheter and were correlated with AF recurrence in 34 (1^{st} study) early cases (ablating 68 superior PVs) and 15 (2^{nd} study) later cases (53 superior and inferior PVs). Total elimination of PV potentials or PV-LA dissociation was achieved in 93% (63/68 PVs) and 93% (49/53 PVs), respectively. During mean follow-up periods of 24.1 ± 4.1 and 13.3 ± 1.7 months, AF recurred in 38% (13/34 cases) and 13% (2/15) in early and later groups, respectively, but no case developed severe PV stenosis. Although the amplitude of PV and periostial LA potentials were decreased ($p < 0.0001$) in all patients, the remaining PV potentials in 34 non-recurrence cases were definitely smaller than those in 15 recurrence cases ($p < 0.0001$). When a cut-off level of less than 0.4 mV in receiver operating characteristic curves was used, its negative predictive value for non-recurrence of AF was 93% and specificity was 95%.

Conclusions: Circumferential ablation around the PV ostia using the RBC is effective in the treatment of AF even in a single session, and AF recurrence may well be predicted by precisely measuring the amplitude of remaining PV-LA potentials.

(J Arrhythmia 2005; 21: 384–397)

Key words: Catheter ablation, Atrial fibrillation, Radio-frequency balloon catheter, Left atrium

Received 14, December, 2004: accepted in final form 5, April, 2005.

Introduction

Electrical disconnection between pulmonary veins (PVs) and the left atrium (LA) by catheter ablation of either the pulmonary veins per se or adjacent LA tissue is now a frequently used therapeutic approach in the treatment of paroxysmal atrial fibrillation (AF).[1–3] However, a high recurrence rate (44%)[2] and frequent complication of PV stenosis have been reported.[4,5] It is quite possible that localization of the foci responsible for AF recurrence at more proximal sites around the PV ostia is a major cause of such a poor performance of conventional ablative techniques.[2] Furthermore, variations of PV anatomy including funnel shaped ostium and early branching are not uncommon, making successful ablation of all the foci difficult.[6,16]

In contrast, surgical isolation of PVs and posterior LA wall around the PV ostium (LA MAZE, RADIAL approach) has yielded better clinical results in patients with paroxysmal or persistent AF and even in many cases of chronic AF.[7,8] These reports suggested that tissues around the PV ostia could play an important role in initiating and perpetuating AF.

Based on such considerations, we developed a novel radiofrequency thermal balloon catheter (RBC), whose unique balloon shape snugly fits around the PV ostium and enables us to circumferentially ablate the entire ostial region.[9,16] Although the results of our preliminary study ablating the ostium of both the right and left superior PVs were quite promising, recurrence of AF has still been observed in certain cases.[16] Since localization of the responsible foci within or around the inferior PVs is suspected as a possible cause of such failures, circumferential ablation of all four PV ostia would then be the next logical step. Hence, it is considered desirable to (1) precisely identify the changes in the electrophysiological properties of the PVs and adjacent LA tissue produced by circumferential ostial ablation, and (2) correlate those findings with success or failure of maintaining sinus rhythm. The present study has been designed to precisely analyze those data in a hope that such information would help us delineate a more effective ablative strategy in the treatment of paroxysmal as well as chronic AF.

Methods

1) Patient Characteristics

The study population consisted of 49 consecutive patients (44 male, 58 ± 10 years old) who were markedly symptomatic with multi-drug-resistant paroxysmal AF. Warfarin was administered to all patients for more than 4 weeks to maintain their international normalized ratios (INR) between 1.5 and 2.5. Eighteen patients had hypertension and 8 had diabetes mellitus. Three dimensional electron beam computed tomography was performed to measure the diameter of each PV ostium, and trans-esophageal echocardiography was carried out to elucidate LA anatomy. Patients with intraatrial thrombi or structural heart disease were excluded

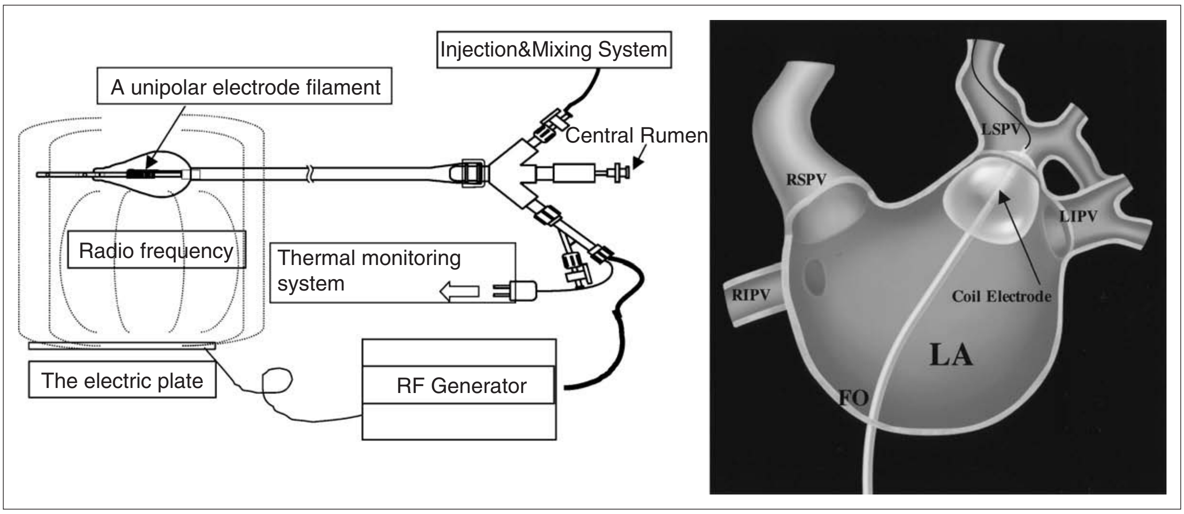

Figure 1 Schema of the novel radiofrequency thermal balloon (RBC) system.
Right panel shows this RBC catheter wedged at the LA-PV junction area, and schematic 3-dimensional view of broad ablation at the junction.
LA: left atrium, LSPV: left superior pulmonary vein, RSPV: right superior pulmonary vein, LIPV: left inferior pulmonary vein, RIPV: right inferior pulmonary vein, FO: foramen ovale.

from the study. All enrolled patients signed an informed consent form approved by the hospital ethics committee.

2) New Device System

As has been described previously, this original RBC (Toray Industries, Inc., Tokyo)[10] is mechanically similar to the one for coronary angioplasty (SST balloon catheter, Japan Crescent). The instrument is composed of an 11F outer shaft, a 4F inner tube and a balloon at the tip. The inner tube can be slid into the main shaft. A 0.035-in. guide wire is inserted into the central lumen of the inner tube through which a contrast medium can be injected. In the space between the inner tube and the outer shaft, there are Teflon-coated leads, which are connected to the thermal monitoring system and the RF current generator, and a tube with a turn-cock used to dilate the balloon with fluid. The tip is equipped with an onion-shaped, semi-compliant balloon with an inflated diameter of either 20, 25 or 30 mm, which is fixed between the distal end of the outer shaft and that of the inner tube (**Figure 1**). The balloon membrane, the shaft and the tube are made of heat-proof, antithrombotic resin. A unipolar electrode filament is coiled around the inner tube inside the balloon to deliver RF energy, along which a thermocouple sensor is mounted to monitor the intraballoon temperature during energy delivery.

3) Electrophysiological Studies Prior to Ablation

In each patient, clinical electrophysiological studies were carried out under antiarrhythmic medication previously ineffective. A decapolar catheter was inserted in the coronary sinus from the right internal cervical vein. Two quadripolar catheters were positioned in high right atrium and close to the His bundle, respectively, via the left femoral vein. In addition, a 16-F soft-tipped sheath was positioned in LA via transseptal approach under intracardiac echocardiograpy (ICE) guidance (EP Technologies, Mountain View, CA, USA). After confirmation of the PV-LA anatomy by selective venography using a guidewire and a custom made catheter (5-F, Medifics Japan, Tokyo) or a 8.5-F sheath for the basket catheter (Boston Scientific, USA) (**Figure 2A**, **3-IA**, **3-IIA**), the most proximal electrode of the basket catheter (31 mm) was positioned at the LA-PV junction (**Figure 2B**, **3-IB**, **3-IIB**). Bipolar intracardiac electrograms were recorded at a filter setting of 30–500 Hz by use of a computerized mapping system (Prucka Cardio Lab: GE Marquette), simultaneously with body surface electrocardiogram (ECG). Endocardial stimulation was achieved with a stimulus intensity of twice to three times the diastolic threshold. For the left superior PV (LSPV), constant burst pacing and the application of premature stimuli were performed from coronary sinus (CS) distally. For the right superior PV (RSPV), pacing in a similar manner was carried out from the right atrial appendage (RAA). If AF was provoked, cardioversion was attempted at least twice. Subsequent ablation was made even in those cases where cardioversion was unsuccessful. Heparin was titrated to maintain an activation coagulation time (ACT) of 250 to 350 seconds. After the electrophysiological study, the basket catheter was replaced by an RBC whose balloon diameter was 5–10 mm larger than that of the PV ostium as determined by selective venography. Those patients with PV ostium diameters smaller than 12 mm were excluded from the study to avoid the complication of PV stenosis.

4) Ablation procedure

After the initial clinical electrophysiological studies, the balloon was wedged at the LA-PV junction. Proper positioning of the balloon was fluoroscopically confirmed by demonstrating that the contrast medium injected into the PV through the central lumen of the inner tube did not leak into the LA. Once such an optimal positioning of the balloon was confirmed (**Figure 2C**, **3-IC**, **3-IIC**), RF current at 13.56 MHz (Medix Generator, Nihon Medix Co., Ltd., Chiba, Japan) was delivered for 3–4 min (early cases) or 4–5 min (later cases) between the coil electrode inside the balloon and the electric plate positioned on the body surface. Intra-balloon temperature was constantly monitored and maintained at 60–67 °C (early cases) or 67–75 °C (later cases) by regulating the output of RF energy ($\sim$200 W). In addition, blood was continuously suctioned from the central lumen of the catheter at a rate of 10 ml/min (early cases) or 5% glucose was infused at a rate of 10–15 ml/min (later cases) using an infusion pump during energy delivery to avoid overheating of the blood in the PV. Because the difference between the temperature of the tissue contacting the balloon membrane and that at the thermal sensor during energy delivery measured 10 to 15 °C in in-vitro studies (unpublished observation), the tissue temperature would have reached 50 to 65 °C during ablation. Also it was able to maintain the balloon temperature uniformly by using the agitation system (**Figure 1**).

5) Electrophysiological Studies After Ablation

Recording of electrograms from the PV and its ostial region was repeated following the RF energy delivery. As sometimes PV potential and LA potentials were confusing even with CS distal or RAA pacing, we defined max voltage as LA-PV junctional potentials before ablation. We stopped the

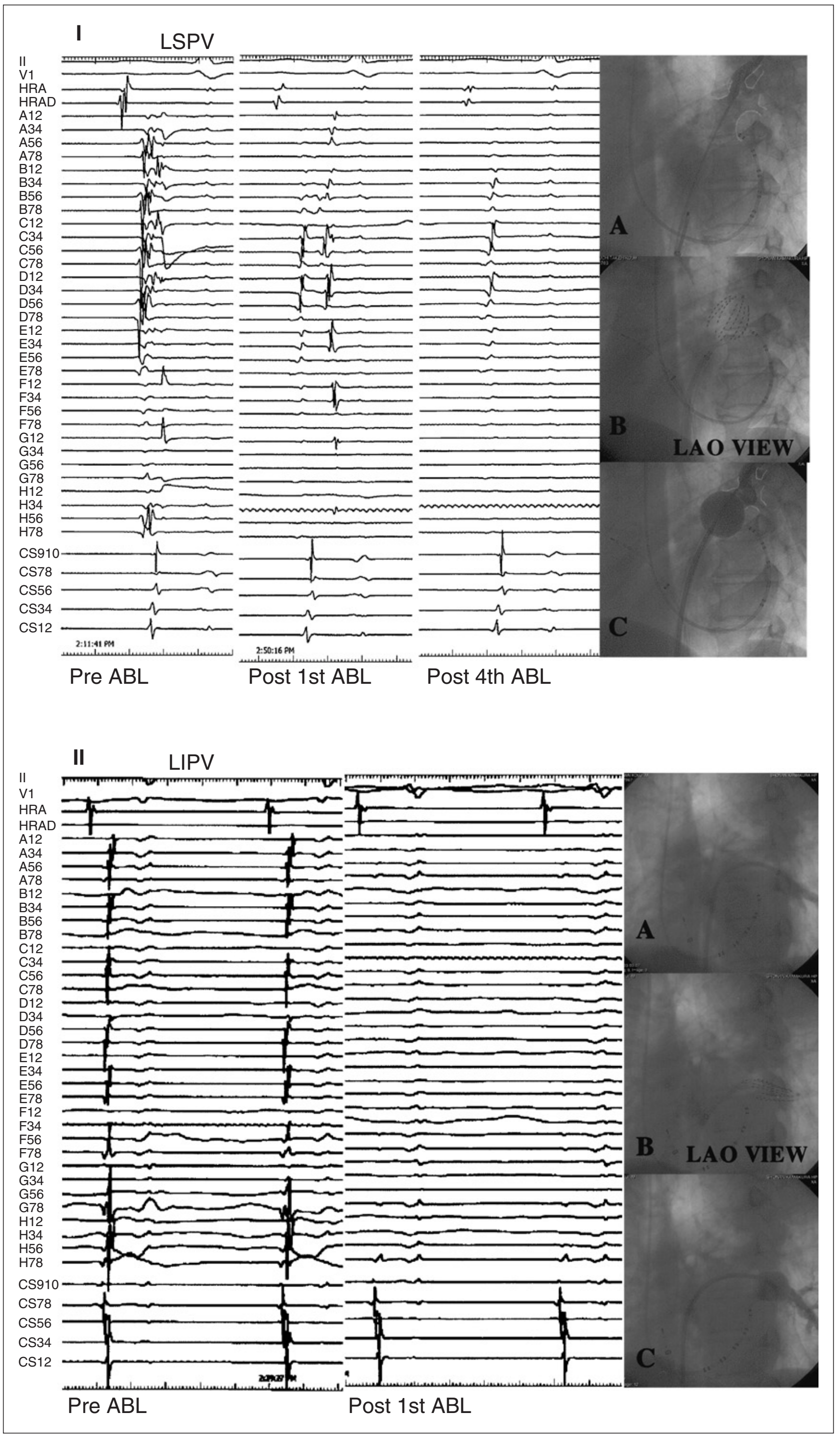

Figure 2
I: Complete elimination of PV potentials (LSPV). After the first ablation, LA-PV interval was prolonged and in the fourth session all PV potentials disappeared completely with significant reduction of LA potentials (far field potentials). A: PV venogram, B: Basket catheter positioned at the LA-PV junction. C: 25 mm balloon was located at the junction.
II: Complete elimination of PV and LA potentials (Annihilation) (LIPV). Note that all PV potentials and almost all LA potentials at the junction have disappeared after ablation. This case maintained sinus rhythm during the follow-up period. C: A 20 mm balloon was set at the junction with a wedge venogram showing no leaks from PV to LA. ABL: ablation.

procedure even though slight PV potentials remained if PV potential elimination or dissociation could not be achieved despite repeated attempts to a maximum of 6 ablations. All procedures for were completed when we could calibrate each maximum PV and adjacent LA potential.

Annihilation was classified as PV potentials or PV and adjacent LA potentials being eliminated completely on all splines of the basket catheter (**Figures 2**, **3**), whereas persistence of PV potential even in only one spline was designated as partial elimination (**Figure 4**).

6) End point

Immediately after the procedure, the RBC was

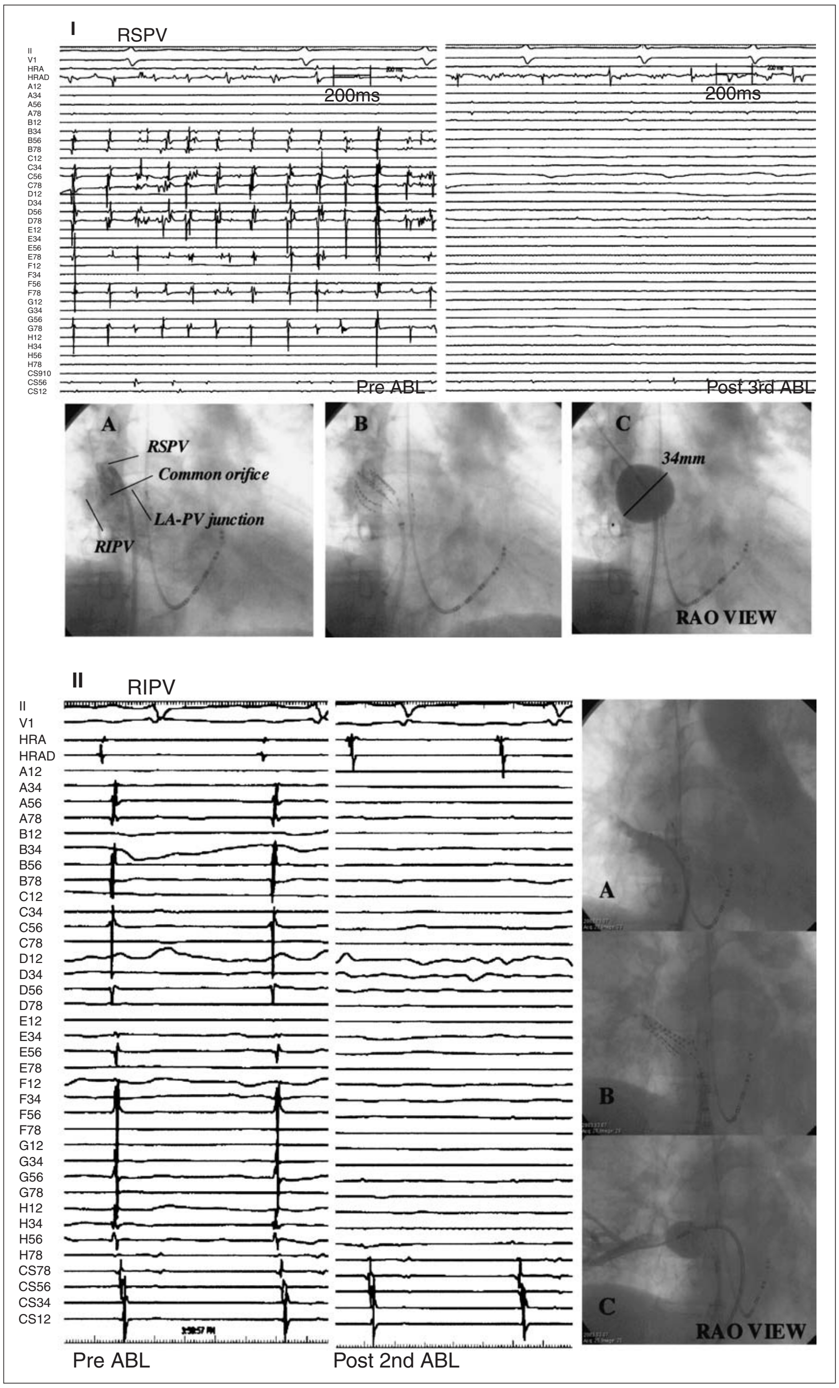

Figure 3
I: Complete elimination of PV and LA potentials (Annihilation) (Common orifice of RSPV and RIPV). The left upper panel shows right PV with common orifice and LA-PV junctional potentials on the basket catheter during atrial fibrillation before ablation. The panel immediately to the right shows complete elimination of all potentials after ablation. A: Angiography of the right PV indicated a common orifice of right superior and inferior PVs. Also note that the anatomical junction between LA and PV was clearly revealed by angiography. B: The basket catheter positioned at the junction between LA and right PV to record the potentials at the orifice area. Note that clear PV potentials could be detected even in the common orifice area. Abbreviations are the same as in Figure 2. C: A 30 mm balloon was positioned at the common orifice of right PV whose diameter was 26 mm, and dilated to maximal size of 34 mm (Max power 140 W, the temperature inside the balloon was 75 °C and ablated two times for a total of 8 min).
II: Complete elimination of PV and LA potentials (Annihilation) (RIPV). Note that all potentials including LA potentials at the junction have disappeared after ablation. This case also maintained sinus rhythm during the follow-up period. C: A 20 mm balloon was set at the junction with wedge venogram showing no leaks from PV to LA. ABL: ablation.

replaced by the basket catheter and the position was fixed as close as possible to that of the pre-ablation study, so that amplitudes of the PV and adjacent LA potentials could be compared between pre- and post-ablation records. When either (1) annihilation of PV potentials or both PV and LA potentials or (2) LA-PV dissociation was confirmed, the procedure was considered successful. Also we stopped the procedure even if slight PV potentials remained after a maximum 6 procedures in each PV.

7) Follow-up

After the procedure, the patients were placed on anticoagulant therapy and their cardiac rhythm was studied by Holter ECG for 48 hours. Holter ECG records were repeatedly obtained at 4 to 6 weeks and 12 weeks following ablation. Antiarrhythmic medi-

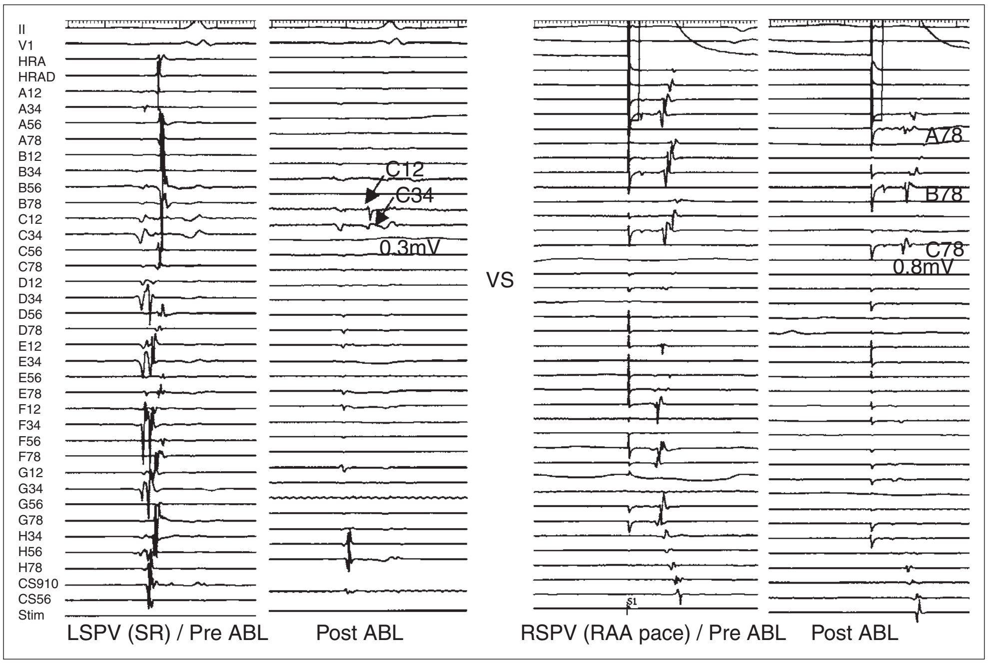

Figure 4 Example of partial Elimination.
The left panel: A discrete PV potential (0.3 mV) in only a solitary C12–34 splint was recognized. This case maintained sinus rhythm during the follow-up period. The right panel: In contrast, a discrete PV potential was recognized in three splints. Note that this potential remained at proximal site of the LA-PV junction. In addition, the amplitude was relatively high (0.8 mV). This was a case involving recurrence.

cation was withdrawn when a patient had no recurrence of AF for 4 to 8 weeks. Contrariwise, those patients who noted the recurrence of symptoms were asked to report the duration and frequency of AF episodes. In addition, all patients underwent 3-dimensional CT of LA and PVs at one, three and six months after ablation.

8) Statistical Analyses

Continuous variables were compared by means of 2-tailed Student's *t* test, whereas χ^2 or Fisher's exact test was used for discrete variables. When the p value was less than 0.05, the difference was considered statistically significant. Then, the relationship between the amplitude of post-ablation PV potentials and late AF recurrence was assessed. The log-rank test was used to compare Kaplan–Meier survival curves in the two (early and later) groups. Receiver operating characteristic curves were used to derive cut-off values for the post-ablation PV potential amplitude that can predict recurrence or non-recurrence.

Results

1) Analysis of Early Cases

In the 34 early cases in which a total of 68 superior PVs were ablated, either annihilation (complete elimination of all PV potentials) or electrical dissociation between LA and PVs was achieved in 41% (28 PVs), whereas partial elimination was seen in 56% (38 PVs). During the follow-up periods averaging 14.1 ± 4.1 months, normal sinus rhythm was maintained in 21 cases (62%), whereas AF recurred in 13 (38%). When details of the ablation procedure were compared between the groups with and without AF recurrence (**Table 1**), no significant differences were noted with regard to the duration of AF prior to ablation, total procedure times as well as total fluoroscopic time.

Contrariwise, total ablation time for LSPV was longer and number of RF energy delivery for LSPV was greater in the non-recurrence group than in the recurrence group. These values were not significantly different between the two groups with reference to RSPVs. It was also evident that a majority of patients in the recurrence group ($22/26 = 85\%$) showed only partial elimination of PV potentials. With reference to the non-recurrence group, on the other hand, complete elimination or LA-PV dissociation was noted in 24 of 40 PVs (60.0%) when the two cases developing atrial flutter during the procedure were excluded. **Table 2** compares post-ablation electrophysiological properties between patients with and without AF recurrence in the early cases. It was found that, for both LSPVs and RSPVs, the

Table 1 Comparison of ablation procedure between patients with and without AF recurrence case (Early cases).

	Recurrence group	Non-recurrence group	*p*
Number of cases	13 (38.2%)	21 (61.8%)	
Number of Pvs	26	42	
Follow up period (M)	14.4 ± 3.5	14.0 ± 4.6	ns
Duration of AF	6.9 ± 6.2	6.1 ± 4.0	ns
Complete elimination (PV)	4	19	p = 0.003#
Partial elimination (PV)	22	16	
PV-LA dissociation (PV)	0	5	
AFL (PV)	0	2	
Total procedure time (min)	135 ± 30 (98–190)	144 ± 30 (110–220)	ns
Total fluoroscopic time (min)	40 ± 10 (28–59)	32 ± 14 (21–72)	ns
Total ABL Time/PV			
LSPV (min)	4.5 ± 2.0	9.2 ± 4.3	p = 0.0008
RSPV (min)	4.0 ± 1.6	5.6 ± 2.7	p = 0.062
No of RF delivery			
LSPV	1.6 ± 0.87	2.6 ± 1.1	p = 0.011
RSPV	1.3 ± 0.48	1.7 ± 0.78	p = 0.100

Fisher's exact test
Follow up period is based upon the period of analysis of early cases before late study

Table 2 Comparison of post-ablation electrophysiological properties between patients with and without AF recurrence case (Early cases).

	Recurrence group N = 13	Non-recurrence group N = 21	*p*
LSPV			
Complete elimination (PV)	2	10	p = 0.024#
Partial elimination (PV)	11	9	
PV-LA dissociation (PV)	0	2	
AFL (PV)	0	1	
Amplitude of remaining potentials			
PV (mV)	1.18 ± 0.92	0.55 ± 0.45	p = 0.013
LA (mV)	0.23 ± 0.12	0.14 ± 0.10	p = 0.017
RSPV			
Complete elimination (PV)	2	9	p = 0.034#
Partial elimination (PV)	10	8	
PV-LA dissociation (PV)	0	3	
AFL (PV)	0	1	
Amplitude of remaining potentials			
PV (mV)	1.11 ± 0.41	0.45 ± 0.45	p = 0.0002
LA (mV)	0.20 ± 0.10	0.12 ± 0.11	p = 0.031

Fisher's exact test

amplitude of remaining PV and periostial LA potentials was significantly smaller in the non-recurrence group.

2) Comparison of Early and Later Cases

Based on the aforementioned observations in early cases, we proceeded to carry out more complete ablation of PV and periostial regions of all four PVs in later cases. Thus, the number of RF energy deliveries to both LSPV and RSPV was increased by an average of 60% and total ablation time was almost doubled (**Table 3**). This caused a marked increase in the percentage of complete elimination to 85% (45 PVs), and decrease in the percentage of partial elimination to 7.5% (4 PVs). Except for the

Table 3 Ablation procedure in early vs. late cases.

	LSPV Early/Late	RSPV Early/Late	LIPV /Late	RIPV /Late
Total ABL Time (min)	7.4 ± 4.3 (3–18)/14.8 ± 7.8 (2–34)	4.9 ± 2.4 (2–12)/10.7 ± 5.6 (2–26)	/9.9 ± 4.3 (3.5–20)	/11.9 ± 4.6 (6.5–21)
No. of RF delivery	2.2 ± 1.1 (1–4)/3.5 ± 1.5 (1–6)	1.5 ± 0.7 (1–3)/2.5 ± 1.2 (1–6)	/2.4 ± 1.0 (1–4)	/2.6 ± 0.7 (2–4)

Fisher's exact test

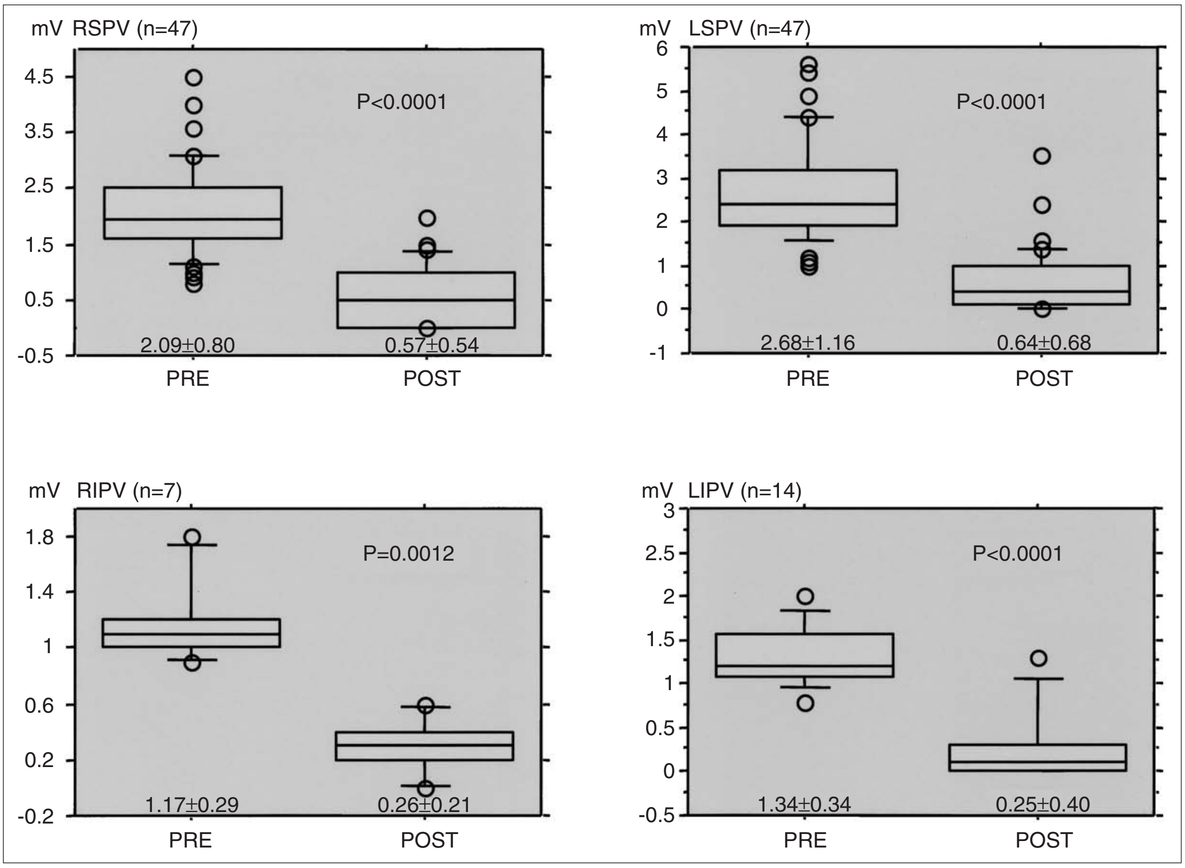

Figure 5 Comparison of LA-PV junctional potentials between pre- and post-PV ablation.
After PV ablation, amplitudes of all PV potentials were significantly decreased as compared to pre-ablation (LSPV: $p < 0.001$, RSPV: $p < 0.0001$, LIPV: $p < 0.0001$, RIPV: $p = 0.0012$).

two patients who developed atrial flutter during the procedure, post-ablation PV potentials were significantly smaller than pre-ablation in individual PVs (LSPV: $p < 0.0001$; RSPV: $p < 0.0001$; LIPV: $p < 0.0001$; RIPV: $p = 0.0012$, **Figure 5**). When the data for all four PVs were combined, post-ablation PV and LA potentials were significantly smaller than pre-ablation ($p < 0.0001$, **Figure 6**). Comparison of the early and later cases revealed that the amplitude of remaining PV-LA potentials in the later cases was significantly smaller than in the early cases (**Figure 7**).

3) Follow-up Results

During mean follow-up periods of 24.1 ± 4.1 and 13.3 ± 1.7 months, AF recurred in 38% (13/34 cases) and 13% (2/15 cases) in the early and later cases, respectively (**Table 4**, **Figure 8**). Twelve of the 13 and 2 of the 2 recurrence cases were from the group of partial elimination. In the early cases, the remaining 21 patients (62%) were free from AF including 16 cases on drugs that were previously ineffective and 5 cases not using drugs. In the later cases, the remaining 13 patients (87%) were free from AF including 2 cases on drugs and 11 cases off drugs. Even in patients with AF recurrence, the frequency and duration of AF episodes were markedly decreased with medication which was previously ineffective. Anyhow the superior results in the present study may due to a combination of drugs and ablation.

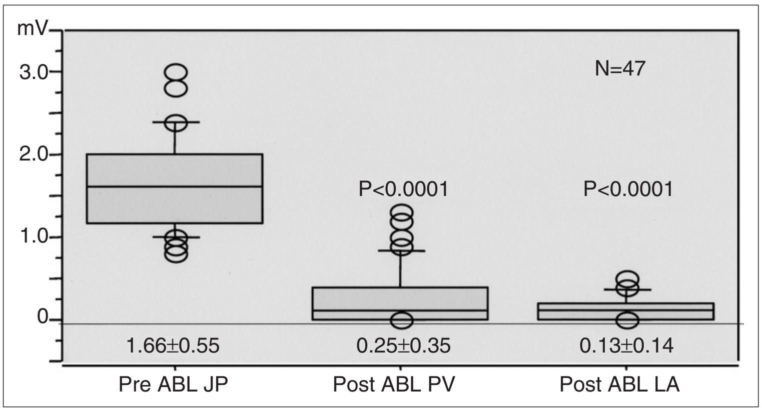

Figure 6 Comparison of LA-PV junctional potentials between pre- and post-PV ablation. All post-ablation PV and LA potentials around PV ostium were significantly decreased as compared to those of pre ablation (Post ABL PV: $p < 0.0001$, Post ABL LA: $p < 0.0001$) versus Pre ABL JP, respectively. ABL: ablation, JP: junctional potentials, PV: pulmonary vein, LA: left atrium.

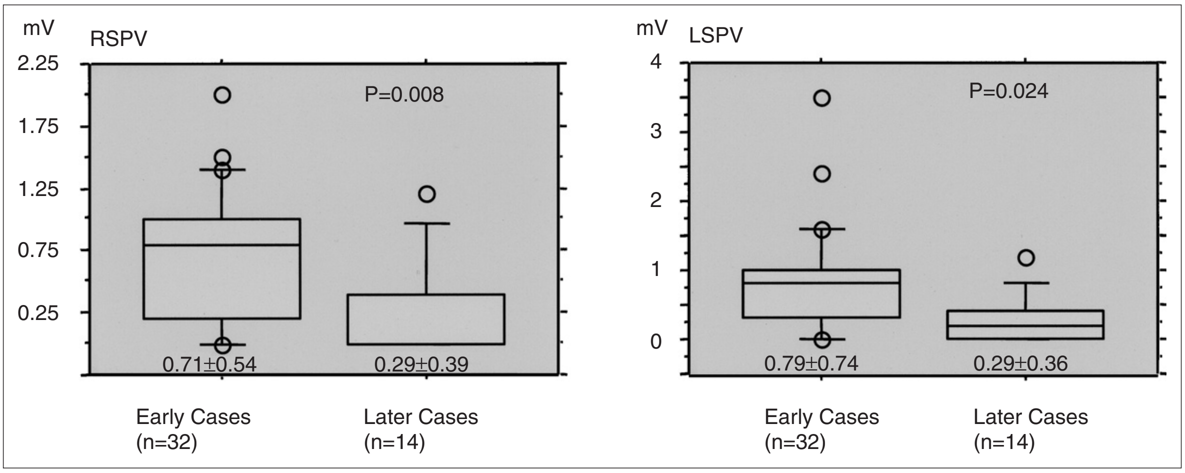

Figure 7 PV potentials just after PV ablation.
PV potentials just after PV ablation in the later cases were significantly lower than those in the early cases (RSPV: $p = 0.008$, LSPV: $p < 0.024$), meaning that we were able to more thoroughly ablate than in the early study. As a result, we obtained more complete elimination (annihilation) in the later cases (83%) than in the early cases (34%). (See Table 4).

Table 4 The results post ablation and follow up data.

	Early cases, N = 34 (2 PVs each, total 68 PVs)	Later cases, N = 15 (3–4 PVs, total 53 PVs)
Complete elimination (PV) (Annihilation)	23/68 = 33.8% (12/34 LSPV, 11/34 RSPV)	44/53 = 83% (13/15 LSPV, 12/15 RSPV, 13/15 LIPV, 6/8 RIPV)
Partial elimination (PV)	38/68 = 55.9% (20/34 LSPV, 18/34 RSPV)	4/53 = 7.55% (1/15 LSPV, 1/15 RSPV, 1/15 LIPV, 1/8 RIPV)
PV-LA dissociation (PV)	5/68 = 7.4% (2/34 LSPV, 3/34 RSPV)	1/53 = 1.9% (1/15 RSPV)
AFL (PV)	2/68 = 2.9% (1/34 LSPV, 1/34 RSPV)	4/53 = 7.55% (1/15 LSPV, 1/15 RSPV, 1/15 LIPV, 1/8 RIPV)
Amplitude of remaining potentials		
PV (mV)	1.18 ± 0.92	0.55 ± 0.45
LA (mV)	0.23 ± 0.12	0.14 ± 0.10
Recurrence	38.2% (13/34)	13.3% (2/15)
Total procedure time (min)	135 ± 30 (98–190)	272 ± 74 (180–420)
Total fluoroscopic time (min)	40 ± 10 (28–59)	77 ± 22 (34–110)
Follow up period (M)	24.1 ± 4.1	13.3 ± 1.7

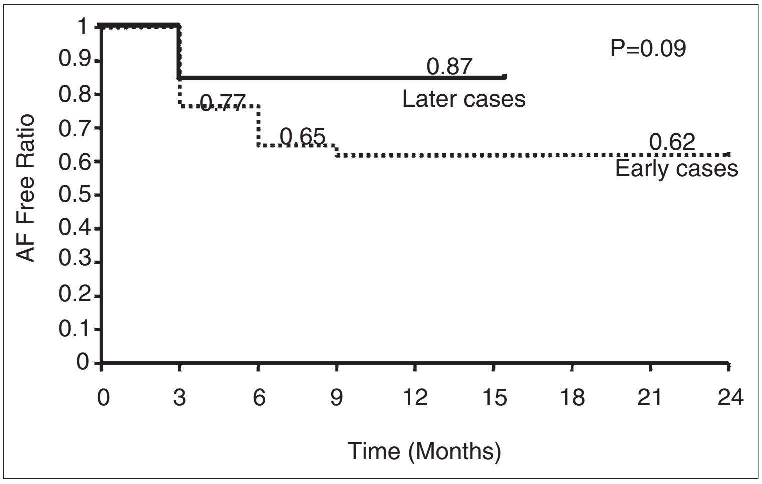

Figure 8 Kaplan–Meier curves for AF free ratio post PV ablation in early and later cases. Although it was not a significant difference between the two groups, in the later cases, 13 patients (87%) were free from AF. Even in patients with AF recurrence, the frequency and duration of AF episodes were markedly decreased with the medication which had been ineffective previously.

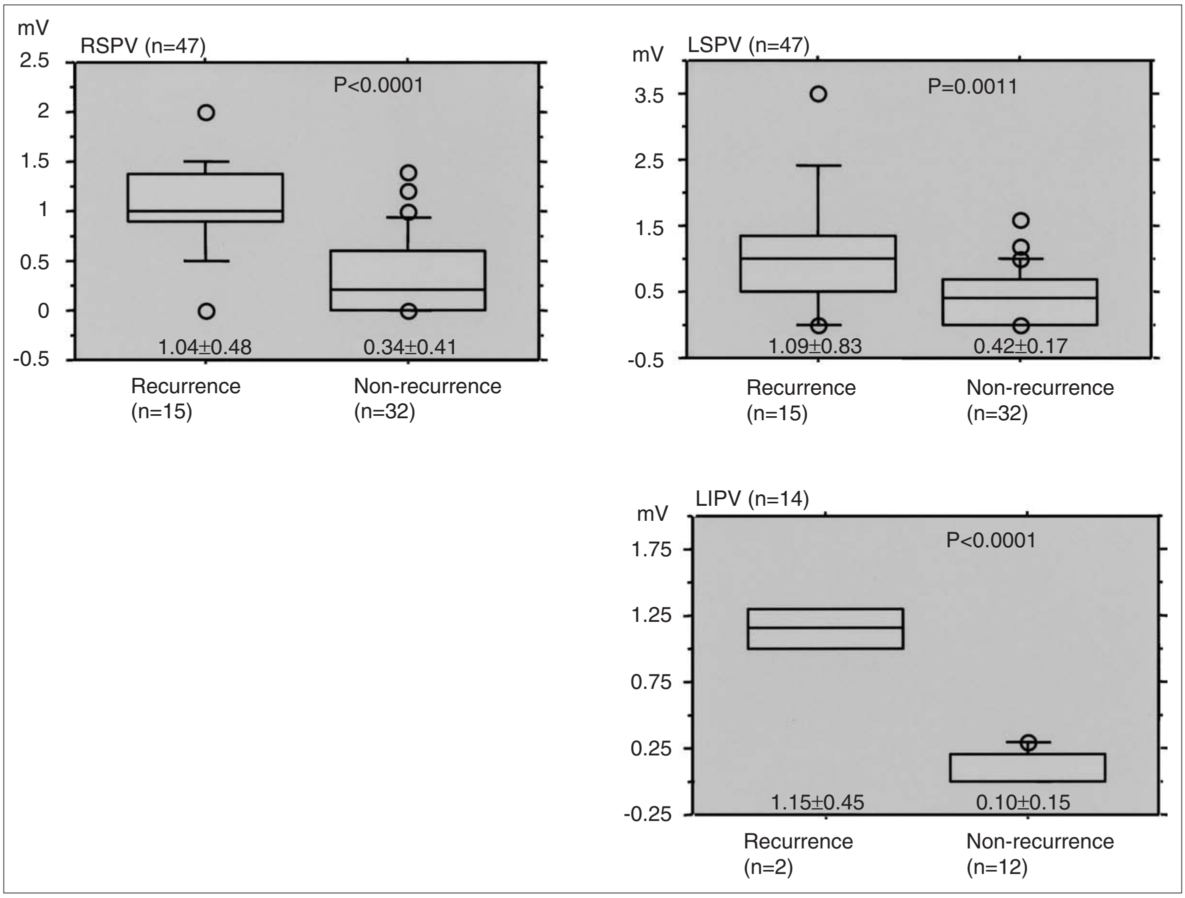

Figure 9 Comparison of post PV ablation LA-PV junctional potentials between recurrence and non-recurrence group. The remaining PV potentials in 32 non-recurrence cases (except for 2 cases developing AFL) were definitely smaller ($p < 0.0001$) than those in 15 recurrence cases.

In all 49 patients, 3-dimensional CT was performed one, three months and six months after the procedure. No evidence of severe PV stenosis was found except for six cases, showing slight shrinkage of the PV ostium in three, mild PV stenosis with 30–50% narrowing in two and 50–60% narrowing in one in a manner consistent with late progression of inferior PV. However, no symptoms were noted in these six cases.

4) Comparison of Remaining Potentials between Recurrence and Non-recurrence Cases

When we compared the amplitude of remaining potentials in PV and periostial regions between the recurrence and non-recurrence groups, the remaining PV potentials in 32 non-recurrence cases (except for 2 cases developing AFL) were definitely smaller than those in 15 recurrence cases ($p < 0.0001$, **Figure 9**). When a cut-off level of less than 0.4 mV in receiver operating characteristic curves was used, its negative predictive value for non-recurrence of AF was 93% and specificity was 95%.

5) Complications

A transient ST segment elevation in inferior ECG leads was noted in 3 patients, most likely as a result of coronary air embolism during catheter exchange. No cerebrovascular accidents were documented during and after the procedure. No clot formation in the catheter was noted. Three patients had minor pericardial effusion after ablation, with one of them requiring a drain. Phrenic nerve paralysis has never been observed following RSPV ablation.

6) Discussion

There have been several reports that electrical PV isolation is a promising therapeutic approach against paroxysmal AF caused by the presence of triggering foci within the PVs.[1–3] In some of the earlier studies, however, the rate of AF recurrence was as high as 44%.[2] Furthermore, it has been pointed out that more proximal portions of the PV-LA junction appear to play an important role, since in 13% of cases with AF recurrence, impulse formation originated more proximally than the first target regions.[2] Based on those considerations, complete PV isolation as a purely anatomical approach has recently been advocated.[11,12] On the other hand, Oral et al. reported that after a complete PV isolation, AF persisted in 40% of cases.[13] They pointed out the possibility that, in addition to the presence of triggering foci in the PVs, many other factors could contribute to the maintenance of AF.[13] It appears especially important to modify the arrhythmogenic substrate in the posterior LA region including the PV ostia, since the Maze operation,[14] surgical PV isolation,[7] radial approach,[8] or radio-frequency ablation during open-heart surgery[15] often produced excellent clinical results.

In this regard, it is likely that the myocardial sleeve of the LA entering into the PVs is thicker at the PV-LA junction, often showing abrupt change in direction.[17] Furthermore, it tends to be more prominent in the superior PVs,[18] and node-like cells with automaticity may also be found around the PV ostium.[19] However, Saliba et al. reported that it was difficult to obtain effective compression of a balloon against the PV ostia with sufficient coaxiality due to the discordant diameters of balloon and PV ostia.[20] In our novel RF balloon catheter system, those problems were solved by adopting a funnel-shaped balloon in different sizes and having sufficient flexibility as well as compliance. As a result, our earlier animal experiments using porcine hearts have shown that this catheter could ablate not only the PV-LA junction, but also the LA tissue around the PV ostia in a manner similar to a surgical encircling incision.[9]

In our initial clinical studies on patients with paroxysmal AF, we ablated only superior PVs. However, fairly good results were obtained despite a high ratio of partial elimination (55.9%).[16] This could probably be explained by the fact that a majority of PV triggers are located in supeior PVs,[3] and the effect of local denervation of the ganglionic plexus around the supeior PV-LA junctions by the ablation.[31] Furthermore, as shown in **Figure 4**, even some cases in the partial elimination group remained in sinus rhythm after the procedure. Our question then was to what extent we should ablate the PV-LA junctional region to prevent the recurrence of AF. Thus, in the later cases, we tried to deliver a grater amount of RF energy to the ostial regions of all four PVs so that possible triggering foci would be more completely isolated. As a result, percentage of annihilation was markedly increased, whereas cases with AF recurrence were reduced as compared to the early cases. Therefore, less procedure time may be associated with higher recurrence of AF. One other significant finding obtained in the present study was that when the amplitude of all the remaining PV-LA potentials was decreased to less than 0.4 mV, non-recurrence of AF could be predicted with high sensitivity and specificity.

7) Safety from Thromboembolism and PV Stenosis

Either continual suction of blood (early cases) or infusion of 5% glucose solution through the central lumen of the catheter (later cases) using a rotary pump during energy delivery allowed us to avoid overheating of PV blood and resultant thrombus formation. Thus, no cases of overt thrombus formation nor episodes of thromboembolism have been observed. On the otherhand, development of PV stenosis caused by overheating of PV wall has been reported as a serious complication of the conventional PV ablation method.[4,5] Delivery of lower energy to avoid such overheating could, however, result in an insufficient ablation. In the present study, no significant PV stenosis was noted even after sufficient energy deliveries except for five cases having a slight distortion of the PV-LA junction and one case having a mild (50–60%) stenosis in 3-dimensional CT. In this regard, it has been reported that PV stenosis was rare when lesions were made more proximal to the ostium.[11] The present balloon circumferentially ablating the ostial regions probably avoided PV stenosis in the same manner. It should also be pointed out that the temperature measured at the conventional catheter tip in contact with the endovascular surface may underestimate deeper tissue temperature since the tip is being convectively cooled by the blood flow,[21] and this may explain the development of PV stenosis at an apparently low temperature in conventional studies. According to a more recent paper, acute heat-induced contraction of PVs was observed at a distal ablation catheter temperature of 60–65 °C. Furthermore, our patient who developed mild stenosis had a relatively small (13 mm) diameter of the inferior PV and ablation was carried out slightly deeper into the PV. Therefore, we should pay special attention to the temperature and catheter position during PV ablation. Fortunately, in the present study, temperature of the tissue in contact with the balloon during ablation was shown to be always lower than that of the balloon membrane (50–65 °C) according to the repeated in vitro and animal experiments. The present method would thus be superior as long as ablation of more proximal regions of the PV-LA junction is achieved with sufficient energy delivery.

8) Withdrawal of Drugs

Needless to say, withdrawal of drugs soon after the procedure would be most advantageous to any patient. However, it has been observed that, during long-term follow-up, some patients with recurrence of AF (especially several weeks after the PV isolation) became responsive to the drug that were previously ineffective. This finding may be explained either by inflammatory changes due to RF energy or by a delayed therapeutic effect.[23] Therefore, we attempt to withdraw drugs carefully to give the patient a better quality of life.

9) Future Perspectives

Several reports have pointed out that the posterior wall of LA near the PV ostia and the left atrial appendage would play an important role in maintaining AF even in patients with chronic AF, since the highest dominant frequency was localized in those areas.[24–26] Gerstenfeld et al. empirically demonstrated proximal isolation of all PVs to reduce future recurrence.[27] Contrariwise, a more recent report indicates that PV isolation may not be a crucial method to maintain sinus rhythm, whereas modification of the posterior LA including the PV ostia could be more important[28] to treat AF. Based on these diverse observations, combination of complete PV isolation and modification of the arrhythmogenic substrate in the posterior LA wall around the PV ostia may well be indicated to achieve better results. It is hoped that our present approach could fulfill these requirements.

10) Study Limitations

The number of patients as well as ablated PVs might be too small to fully evaluate the efficacy of this treatment using the RBC system. Since the follow-up period was too short particularly in later cases, it could not be concluded that PV stenosis would not occur. To date, however, no severe PV stenosis with symptoms has been documented. Since we did not carry out electrophysiological restudy of all cases with AF recurrence, it cannot be determined whether it relapsed from the ablated region or from certain new foci in the LA, SVC, Marshall vein, and so forth. Furthermore, we could not be certain that the patients without recurrence did not receive higher voltage at follow-up. However, there are many ethical issues, at least in Japan, in putting innocent patients who have regained their sinus rhythm at potential risk by performing electrophysiological studies. It must also be pointed out that, although a basket catheter is one of the most widely accepted devices to record PV potentials,[24,29] the recorded potentials may not always represent direct potentials of LA, but may reflect some far-field potentials, such as possible non-recurrence cases with remaining potentials actually recording some far-field potentials such as that of the left atrial appendage or HRA.

Hence, further improvement of the basket catheter or the development of a new device for recording direct LA potentials around the PV ostium may be necessary to confirm the range of ablation. It is difficult to conclude that our RBC system could completely eradicate the AF, since the occurrence of short periods of non-symptomatic AF was not ruled out. Therefore, we should continue the anti-coagulation therapy carefully at least for one year after the procedure in view of the results in the AFFIRM study.[30] A multi-center clinical trial is now in progress to more precisely evaluate the efficacy of this catheter system.

Conclusions

It is concluded that this novel balloon catheter could ablate not only the PV-LA junction, but also adjacent LA tissues around the PV ostia circumferentially without the risk of PV stenosis or thromboembolism. The rate of AF recurrence was extremely low, when both the superior and inferior PVs were isolated and a marked decrease in the amplitude of LA-PV potentials to less than 0.4 mV was obtained. Finally, we would like to emphasize that circumferential ablation around the PV ostium using this RBC system could achieve the equivalent therapeutic effect to that of conventional ablation, even in a single session.

Acknowledgements

This work was supported by a Research Grant for Cardiovascular Diseases (14C-2) from the Ministry of Health, Labor and Welfare.

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